Annals of Clinical and Analytical Medicine
Original Research

Efficacy of shear wave elastography in malignity assessment of thyroid nodules with atypia of undetermined significance and comparison with TI-RADS

Elastography of undetermined thyroid nodules

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Abstract
Aim: The aim of this study is to investigate the effectiveness of shear wave elastography (SWE) in the differentiation of benign-malignant thyroid nodules diagnosed with atypia of undetermined significance (AUS) and to compare with the American College of Radiology (ACR)-thyroid imaging reporting and data system (TIRADS).
Material and Methods: This monocentric study comprised 52 patients (9 males; 43 females) who were diagnosed with AUS by thyroid FNAB. All patients included in the study had gray scale ultrasound (US) and SWE images. The mean SWE value was calculated for each nodule, and TIRADS scores were determined based on the US. The obtained data were compared based on the histopathological result in patients who had undergone surgical treatment, and based on the cytology result in patients followed-up by FNAB, for the differentiation of benign and malignant nodules.
Results: Nineteen patients were found to have malignant nodules and 33 had benign nodules. The mean SWE was 2.89±0.51 (2.30–3.92) and 2.91±0.48 (2.16–3.79) in the malignant and benign cases, respectively. The results of independent T- tests between the two groups were insignificant (p=0.89). TIRADS 2-3 (total 29 patients) nodules were considered possibly benign, and TIRADS 4-5 (total 23 patients) possibly malign, the sensitivity, specificity, positive predictive and negative predictive value of TIRADS were identified 100%, 87.9%, 82.6% and 100%, respectively, when compared with the pathology results.
Discussion: There was no significant difference in SWE values in the differentiation of malignant-benign thyroid nodules with AUS. However, the ACR-TIRADS criteria still maintain their importance.

Keywords
Elastography, Thyroid nodule, Undetermined, TI-RADS, Ultrasonography

DOI: 10.4328/ACAM.20949 Received: 2021-11-14 Accepted: 2021-12-16 Published Online: 2022-01-25 Printed: 2022-02-01 Ann Clin Anal Med 2022;13(2):215-219
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Introduction

Thyroid nodules are among the most frequently encountered pathologies in routine daily practice, both clinically and radiologically, and should be considered clinically important due to the roughly 5% risk of malignancy [1-3]. In this regard, the assessment of suspicious nodules is important to avoid unnecessary surgery. Fine needle aspiration biopsy (FNAB) has played a significant role in patient selection for surgery since it was accepted as the optimum approach for the differentiation of benign and malignant nodules [4-6]. However, a major limitation of FNAB is that it results in undetermined cytology in around 20–25% of cases [7, 8]. Although generally, a surgical approach is recommended for the treatment of such nodules, histological evaluation of this type of nodule in more than 70% of cases results in a benign pathology [4, 9]. Another approach is to follow-up such nodules with atypical cytology with FNAB, since most of them are benign [10]. Hence, the management of patients with undetermined cytology can be considered challenging. Considering these data, there is still a need to come up with better approaches to the preoperative diagnostic evaluation of patients with undetermined cytological findings in fine needle biopsy.

Ultrasound elastography is a newly developed technique that is gaining broader use day by day. Sonoelastography, based on the hardness of malignant tissues when compared to benign tissues, can be accepted as a sonographic equivalent of palpation as a common approach in physical examinations [11]. It is possible to be informed of the hardness of the organ or nodule from the superficial location of the thyroid gland. Strain wave elastography provides qualitative or semi-quantitative values and is operator dependent; while ARFI, transient and shear wave elastography present quantitative values, and is less operator dependent. Shear wave elastography (SWE) is a technique in which a pushing pulse is sent through the screening axis, advancing perpendicular to the screening axis, and which works based on the measurement of the velocity of the waves referred to as shear waves. Shear waves move faster through hard tissue, since velocity is associated with tissue stiffness [12-14]. It is possible to identify quantitatively the level of tissue stiffness based on the shear wave elastography. In this study, we aimed to compare the effectiveness of shear wave elastography technique in the differentiation of benign and malignant thyroid nodules diagnosed with atypia of undetermined significance by FNAB, and to compare it with the American College of Radiology (ACR)-thyroid imaging reporting and data system (TIRADS).

Material and Methods

Patients

Approval for the study was granted by the ethics committee of the institution, and written informed consent was obtained from all participating patients (2021/10-13). The records of 318 patients diagnosed with atypia of undetermined significance by thyroid FNAB in the interventional radiology clinic between January 2017 and August 2021 were screened retrospectively. Among these patients, those whose ultrasound and ultrasound elastography images were retrievable from the PACS (Picture Archiving Communication System) and who had a histopathological result or diagnosis of benign or malignant thyroid nodule during follow-up FNAB were included in the study. After the exclusion of 169 patients with missing ultrasound and ultrasound elastography images, 32 patients with a whole or partially cystic or calcified nodule, and 65 patients with missing follow-up FNAB or histopathological results, the study was completed with 52 patients matching the inclusion criteria.

Imaging

All patients included in the study had gray scale ultrasound and ultrasound elastography images obtained by the same radiologist with 13 years of experience prior to the FNAB. Ultrasound and elastography evaluations were performed using a Siemens ACUSON S2000™ (Siemens Healthcare, Erlangen, Germany) device. ARFI elastography evaluations were performed using a 4–9 MHz 9L4 linear probe and the Virtual Touch IQ (Virtual touch-operated IQ) option. First, a gray scale ultrasound evaluation was performed with the patient in the supine position. According to the TI-RADS system [15], five features of each nodule were evaluated, including (1) component (choose one): cystic or almost completely cystic 0; spongiform 0; mixed cystic and solid 1; solid or almost completely solid 2; (2) echogenicity (choose one): anechoic 0; hyperechoic or isoechoic 1; hypoechoic 2; very hypoechoic 3; (3) shape (choose one): wider-than-tall, 0; taller-than-wide, 3; (4) margin (choose one): smooth 0; Ill-defined 0; lobulated or irregular 2; extrathyroid extension 3; and (5) echogenic foci (choose one): none or large comet-tail artifact 0; macrocalcification 1; peripheral (rim) calcification 2; punctate echogenic foci 3. Each feature was assigned a corresponding score, and then the nodules were assigned to different TIRADS categories according to their total scores. Nodules with score 0 were classified as TI-RADS category 1 (malignancy risk of 2%, benign), score 2 was classified as TIRADS category 2 (malignancy risk of 2%, probably benign), score 3 was classified as TI-RADS category 3 (malignancy risk of 5%, mild suspicious malignancy), scores 4 to 6 were classified as TI-RADS category 4 (malignancy risk of 5–20%, moderate suspicious malignancy), and scores ≥7 were classified as TI-RADS category 5. Thereafter, elastography measurements were made using the SWE technique. The patients were told not to breathe deeply, cough, strain or move during the procedure. The linear probe was held as stable as possible, and gel was applied between the skin and the probe so as not to put pressure on the thyroid nodule. Two windows were opened on the screen using the dual key, and the borders of the nodule were drawn manually on the left-hand window (gray-scale US). The borders of the same nodule were produced automatically by the device on gray-scale color-coded elastography images (Figure 1-A). The ROI (region of interest), the dimensions of which were produced automatically by the device and which give the shear wave velocity at the nodule borders, were added to the right-hand image (elastography) (Figure 1-B). Although the number varies according to the size of the nodule, at least 5 ROIs were placed to obtain a more reliable mean value.

The mean of shear wave velocity was calculated for each nodule in m/sec, and the TIRADS scores were determined based on the gray-scale US properties. In nodules with atypia of undetermined significance, the obtained data were compared

based on the histopathological result in patients who had undergone surgical treatment, and based on the cytology result in patients followed-up by FNAB, to differentiate between benign and malignant nodules.

Statistical Analysis

The descriptive statistics for continuous variables in the study included mean, standard deviation, and minimum and maximum, while categorical variables were expressed as numbers and percentages. An Independent samples t-test was performed to compare group means for continuous variables, and a Chi-square test was performed to determine the association between the groups and categorical variables. An independent sample T test was used to compare the mean shear wave values between malign and benign groups. Sensitivity, specificity, positive and negative predictive values were calculated using TI-RADS 2, 3 for benign lesions, and TI-RADS 4 and 5 for malignant lesions. The level of statistical significance was set at 5% in the calculations, and the SPSS software package was used for all statistical analyses.

Results

A total of 52 patients (9 males; 43 females) with atypia of undetermined significance in the thyroid nodule were included in the study. The diagnosis of 26 patients (10 benign, 16 malignant) was confirmed by histopathology, and of another 26 patients (23 benign, 3 malignant) with follow-up FNAB. According to the histopathology or follow-up FNAB, 19 patients (36.5%) were identified with malignant and 33 (63.5%) with benign nodules. Among patients with malignant nodules, five were male and 14 were female, with an average age of 47±10.6 years (age range: 33–75). Among patients with benign nodules, 4 were male and 29 were female, with an average age of 40±12.6 years (age range: 22–65).

The mean SWE was 2.89±0.51 (2.30–3.92) and 2.91±0.48 (2.16–3.79) in the malignant and benign cases, respectively. The results of independent T- tests between the two groups were not significant (p=0.89). According to the gray-scale US findings, 11 patents were classified as TIRADS 2, 18 as TIRADS 3, 17 as TIRADS 4 and 6 as TIRADS 5 (Figures 2, 3). All the TIRADS 2 and 3 nodules, identified from histopathology or follow-up FNAB, were benign; all the TIRADS 5 nodules were malignant, and four of the TIRADS 4 nodules were benign and 13 were malignant (Table 1). The nodules identified as TIRADS 2 and 3 (total 29 patients) were accepted as possibly benign, and the TIRADS 4 and 5 nodules (total 23 patients) were accepted as possibly malignant, and were compared with the histopathology results or follow-up FNAB results. Considering pathology (histopathology or cytology) results as the optimum approach to the determination of malignancy, the sensitivity, specificity, positive predictive value (PPV) and negative

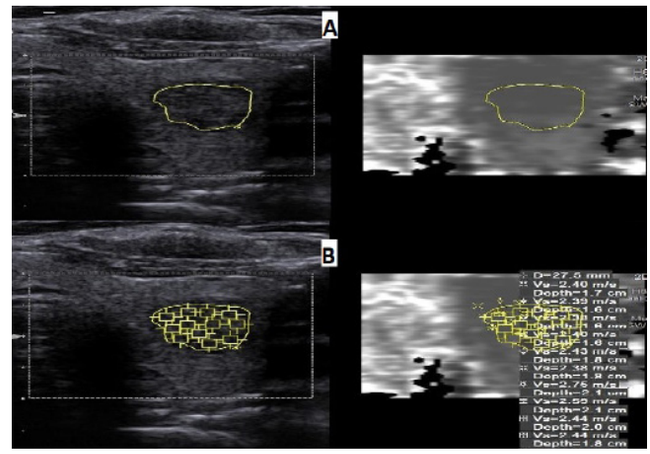

Figure 1. A) Manually delineated nodule in the left window, device-generated borders in the right window (elastogram). B) ROIs that give the SWE velocity of nodule.

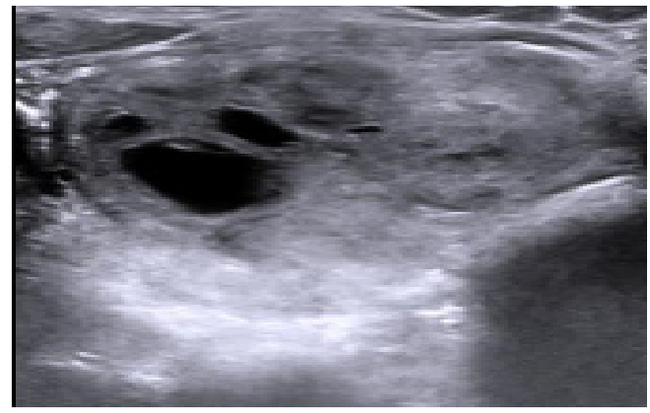

Figure 2. US features of a nodule with AUS, which is benign in follow-up FNAB; mixed cystic and solid (1 point), isoechoic (1), wider-than-tall (0), smooth margin (0), none echogenic foci (0). It was classified as TI-RADS 2

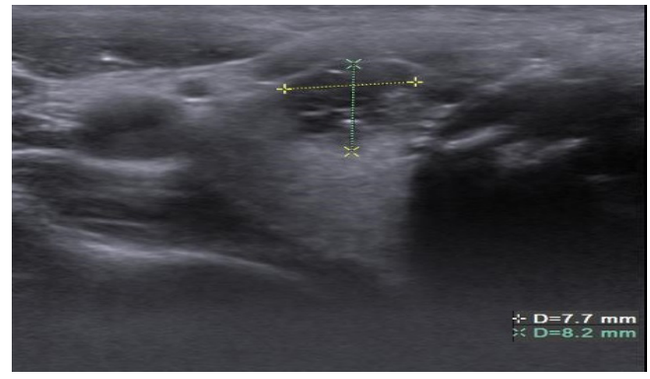

Figure 3. US features of a nodule with AUS, which is malign in histopatology; solid or almost completely solid (2 point), hypoechoic (2), taller-than-wide (3), lobulated or irregular (2), none echogenic foci (0). It was classified as TI-RADS 5.

Table 1. TI-RADS categories and overall diagnostic performance.

TI-RADS	Malign (n)	Benign (n)	Total (n)	Senstivity	Specifity	PPV	NPV
2	0	11	29	100%	%87.9	%82.6	100%
3	0	18					
4	13	4	23				
5	6	0					

predictive value (NPV) of TIRADS were identified 100%, 87.9%, 82.6% and 100%, respectively.

Discussion

The main goal in the evaluation of the thyroid nodules is to determine precisely whether the nodule is benign or malignant, and thus decrease the need for unnecessary FNAB and surgery. Although fine needle aspiration biopsy is the most accurate approach to the characterization of thyroid nodules, the main limitation of this diagnostic approach is the possibility of a result of atypia of undetermined significance. Accordingly, a diagnostic approach that differentiates between benign and malignant nodules without the need for surgery in atypical nodules gains importance.

There have been various studies to date reporting equivocal results in the differentiation of malignant and benign thyroid nodules with atypia of undetermined significance. Malignant nodules have been found to have a statistically higher level of stiffness than benign nodules in a strain elastography studies of 270 (81 malignant and 189 benign) nodules [16], 140 (40 malignant and 100 benign) nodules [17] and 45 (13 malignant and 32 benign) nodules [18]. In a study performed using positron emission tomography (PET), multiparametric US (MPUS) and scintigraphy in 87 patients with atypia of undetermined significance that were histopathologically confirmed to be benign and malignant in 69 and 18 cases, respectively, the sensitivity, accuracy and negative predictive value (NPV) of PET were found to be significantly higher than that of MPUS and scintigraphy [19]. The strain elastography among the MPUS parameters, when evaluated alone, was found to have a suboptimal accuracy in differentiating between the malignant and benign character of thyroid nodules with atypia of undetermined significance. In another study [20], it was concluded that the preoperative strain elastography of thyroid nodules had low elasticity in most of the nodules, and was confirmed not to be so beneficial in the preoperative diagnosis of thyroid nodules with undetermined cytology, in contrast to the recent reports stating them to be beneficial. In contrast to previous studies of the strain elastography approach that revealed qualitative or semi-quantitative data, the SWE technique with quantitative values and less dependent on the operator was used in the present study. No statistical difference was found between benign and malignant nodules in the present study, which may be attributable to the low number of cases, and especially the low number of malignant cases. We also did not find a significant difference in elasticity in these nodules, which are not always cytologically distinguishable.

A significant difference was seen between strain elastography values recorded for benign and malignant nodules in a study [21] performed using both strain elastography and SWE on thyroid nodules with atypia of undetermined significance (P=0.05), while no significant difference was noted in the SWE values of the malignant and benign nodules (P=0.20). It has been suggested that SWE is of no value in differentiating between malignant and benign pathologies, with the nodules in the two groups being reported to have a similar degree of stiffness in a study of 131 thyroid nodules with atypia of undetermined significance [22]. In the present study, in which the applied SWE technique was similar to the studies mentioned above, no significant difference was found in the shear wave values of benign or malignant thyroid nodules with atypia of undetermined significance. Not all of the patients included in the present study had histopathological results, and the acceptance of the follow-up FNAB results as the reference value in some patients may have affected the results. Another SWE study involving a similar patient group reported no benefit of gray-scale US or doppler findings in diagnoses of malignancy, although SWE was reported to be of value in the evaluation of preoperative malignancy risk [23]. Contrary to this study, no significant difference was found in the SWE values in the present study, while the ACR-TIRADS criteria based on the gray-scale US were found to have a high sensitivity and high specificity in the benign and malignant differentiation of thyroid nodules with atypia of undetermined significance.

The main limitation of the present study was the lack of histopathological results of some patients, while a further limitation was the small sample size.

Conclusion

No significant difference was found in the SWE values of benign and malignant thyroid nodules with atypia of undetermined significance. However, the ACR-TIRADS criteria, based on gray-scale US findings, still maintain significance in the differentiation between benign and malignant nodules. Contradictory results have been recorded in the literature based on both SWE and strain elastography approaches to the differentiation of benign and malignant thyroid nodules with atypia of undetermined significance, therefore, further studies involving larger patient series are required. Elastography results should be evaluated concomitantly with gray-scale US findings, even if there are studies with significant results.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Funding: *None*

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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How to cite this article:
Fatma Durmaz, Mesut Özgökçe, Sercan Özkaçmaz, İlyas Dündar, Murat Alay, Cemil Göya, Mehmet Çetin Kotan. Efficacy of Shear Wave Elastography in Malignity Assessment of Thyroid Nodules with Atypia of Undetermined Significance and Comparison with TI-RADS. *Ann Clin Anal Med 2022;13(2):215-219*